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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/475,470 06/07/95 SAMULSKI

R 115132-4

HM12/1123

EXAMINER

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600 GRANT STREET, 42ND FLOOR  
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MOSHER, M

ART UNIT	PAPER NUMBER
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1643

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DATE MAILED:

11/23/99

Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks**

<b>Office Action Summary</b>	Application No. <b>08/475,470</b>	Applicant(s) <b>Samulsi et al</b>
	Examiner <b>Mosher</b>	Group Art Unit <b>1643</b>

Responsive to communication(s) filed on 9/2/99

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle* 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claim

Claim(s) 1, 4, 7-12, 16, 17, 19-21, 25-33, and 36-48 is/are pending in the application.  
Of the above, claim(s) 36-38 and 40-45 is/are withdrawn from consideration.

Claim(s) \_\_\_\_\_ is/are allowed.

Claim(s) 1, 4, 7-12, 16, 17, 19-21, 25-33, 39, and 46-48 is/are rejected.

Claim(s) \_\_\_\_\_ is/are objected to.

Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None of the CERTIFIED copies of the priority documents have been  
 received.  
 received in Application No. (Series Code/Serial Number) \_\_\_\_\_  
 received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of References Cited, PTO-892  
 Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_  
 Interview Summary, PTO-413  
 Notice of Draftsperson's Patent Drawing Review, PTO-948  
 Notice of Informal Patent Application, PTO-152

**-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --**

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***Claim Objections***

Claim 32 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Since claim 32 involves a coding sequence from the human globin gene cluster under the control of a sequence from the human globin gene cluster, the vector of claim 32 does not appear to have the heterologous regulatory sequence required by parent claim 27.

***Claim Rejections - 35 USC § 112***

Claims 27, 31, 33, 39, and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the full scope of the claimed invention, or in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the full scope of the invention. This is a modification of the previous rejection. Applicant convincingly argues that those skilled in the art were aware of usable tissue-specific regulatory elements, including those active in pancreatic, lymphoid, oligodendrocyte, and muscle cells. However, these claims call for a promoter which regulate cell-specific expression in human primary hematopoietic cells. The specification teaches only the globin gene cluster regulatory elements with this specificity, and applicant's arguments do not indicate prior knowledge of other

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regulatory elements with the specificity required for these claims. For these reasons, adequate written description of the regulatory sequences specific for human primary hematopoietic cells is seen as limited to the regulatory elements of the human globin gene cluster.

***Claim Rejections - 35 USC § 103***

Claims 1, 4, 7-12, 16, 17, 19, 20, 21, 25-32, 39, 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walsh et al (1991) in view of Shenk et al 5,436,146, optionally further in view of Ohi et al. This is a modification of the rejections of record, in response to applicant's amendments specifying a heterologous cis-acting regulatory sequence or the absence of a selectable marker. Shenk et al explicitly suggests using an expression control region which controls tissue-specific expression of a foreign gene, see the discussion at column 10, lines 14-46. It would have been within the ordinary skill of the art to combine any member of the group of tissue-specific control elements taught by Shenk et al, including the heterologous lymphoid-cell-active elements, with the wild-type coding sequence taught by Walsh et al, for purposes of expressing the coding sequence in the appropriate tissue. Shenk et al also states that a marker gene "may be desirable" in a recombinant AAV vector, clearly indicating that a marker gene is optional, not mandatory. One of ordinary skill in the art would have been motivated to omit an optional marker gene for reasons such as to insert a larger foreign sequence in an AAV vector. In addition, Ohi et al teaches an example of an AAV vector which does not contain a selectable marker, indicating that omission of selectable marker was known in the AAV vector art. Therefore, the invention as a whole is seen as *prima facie* obvious.

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Claim 33 is rejected under 35 U.S.C. 102(b) as being unpatentable over Walsh et al (1993), in view of Shenk et al 5,436,146. This is a modification of the rejections of record, in response to applicant's amendments specifying a heterologous cis-acting regulatory sequence. Shenk et al explicitly suggests using an expression control region which controls tissue-specific expression of a foreign gene, see the discussion at column 10, lines 14-46. It would have been within the ordinary skill of the art to combine any member of the group of tissue-specific control elements taught by Shenk et al, including a globin gene control region, with the wild-type coding sequence taught by Walsh et al, for purposes of expressing the coding sequence in the appropriate tissue. Therefore, the invention as a whole is seen as *prima facie* obvious.

### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196 .

November 22, 1999

*Mary E. Mosher*  
MARY E. MOSHER  
PRIMARY EXAMINER  
GROUP 1600  
1600